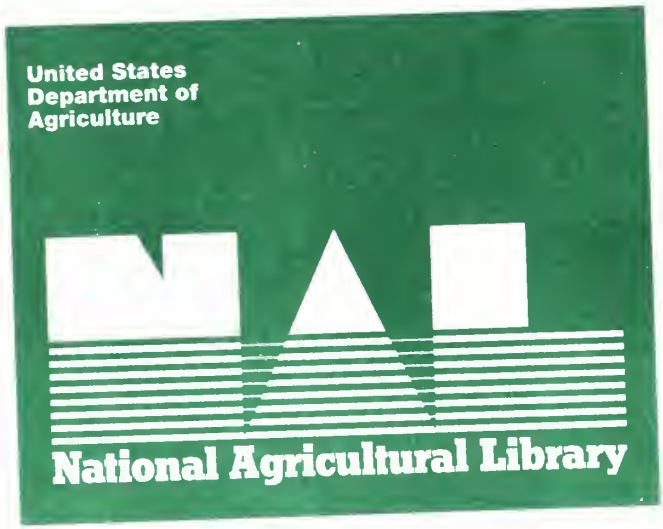
Evaluation of the Children's Nutrition Research Center

Achievements of Ten Years

United States Department of Agriculture

Baylor College of Medicine

Texas Children's Hospital


United States
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EVALUATION OF THE CHILDREN'S NUTRITION RESEARCH CENTER

Achievements of Ten Years

Houston, Texas
1990

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PREFACE

The Children's Nutrition Research Center (CNRC) is a mission-oriented United States Department of Agriculture (USDA)/Agricultural Research Service (ARS) laboratory operated by Baylor College of Medicine through a cooperative agreement. The Texas Children's Hospital has been closely associated with the Center. An important component of CNRC management has been an evaluation of the research conducted in the Center. External review has been incorporated at each level of research program management. The individual project statements, which are the basic units of Center science management, are reviewed by scientists outside the Center according to Agricultural Research Service procedures. The management of Center research has been reviewed annually by groups of nutrition experts. The Council of Scientific Advisors, composed of men and women who are internationally recognized nutrition scientists, has conducted 14 reviews. For the past three years, nutritionists from industry have participated in the Council meetings to evaluate the relevance of Center work to industrial research requirements. Every three to four years, the USDA invites a group of scientists to review and evaluate the compliance of CNRC research to the USDA mission. A group of Baylor College of Medicine departmental chairmen has also been appointed as advisors and has participated in the Council meetings. In addition, a representative from the National Institutes of Child Health and Human Development has attended each meeting to assure coordination between CNRC programs and the NICHD. The proceedings at each Council meeting are transcribed and reports from the Council are circulated to the leadership of the Agricultural Research Service and Baylor College of Medicine.

Those who administer the CNRC, from individual scientists to governing bodies, have agreed that evaluations of Center research are a priority. Many procedures are used to evaluate scientific research; the most familiar to health scientists in the United States is that exercised by the National Institutes of Health for extramural program proposals, i.e., ex-ante evaluation or peer review. The National Institutes of Health, however, in their intramural programs and through a contract mechanism (whereby requests for specific proposals are solicited), modify the review process to one of merit review. The emphasis in both external and internal research evaluation is on the formulation of research protocols. Although attention is given to research accomplishments at the time of competitive renewal, the greatest emphasis remains focused on the formulation of research plans.

Research in progress is also evaluated by external review. Ex-post evaluation determines accountability and the fulfillment of stated objectives. This is common practice in university departments in which the external review process assures that academic standards are being maintained. Organizations such as the NIH use ex-post evaluation to determine whether the scientific results have been worth the investment.

It was within the context of ex-post evaluation that the administrators of the CNRC requested a 10-year review. The review had two objectives: 1) to assure Baylor College of Medicine and the Agricultural Research Service of the USDA that scientific and academic performance and standards are maintained by the CNRC and 2) to evaluate the relevance of CNRC research programs to the original mandate. The review was to be focused at the Center level. The efficiency of program management was to be evaluated and compared with that of similar Centers within the United States and Europe.

The committee was asked to review Center publications, analyze citations, and review the process of Center management. Particular emphasis was to be given to managerial performance, program execution, and the fulfillment of Baylor College of Medicine and the Agricultural Research Service expectations. The innovative quality and multidisciplinary nature of the research was to be evaluated. To this end, interviews were to be conducted with various academic administrators at Baylor College of Medicine and science managers in the Agricultural Research Service. Additional interviews were held with persons in industrial groups and federal agencies who are recipients of CNRC research findings.

The committee was also asked to review 1) the relevance of research findings to business and federal users of the information, 2) the contribution of the Center to Baylor College of Medicine recruitment efforts, and 3) Center contributions to global nutrition.

I wish to acknowledge the leadership and support of ARS officers, Drs. Floyd Horn and Gerald Combs, and Baylor College of Medicine administrators, Drs. Ralph D. Feigin, and William T. Butler. In addition, I wish to thank the following CNRC staff, Norma J. Hayley (Biostatistics), Patricia A. Williams (Metabolic Research Unit), E. Roseland Klein (Publications/Illustrations), Veda N. Nichols (Library), and Jimmy Goodman (ARS).

Buford L. Nichols
Director, CNRC

PART I. Origins and Achievements

1. Introduction

1.1. This review was initiated by the Director as an assessment by independent outside scientists. The authors of the present evaluation are the current members of the Council of Scientific Advisors (CSA):

Lewis A. Barness	(Madison, Wisconsin)
Gilbert B. Forbes	(Rochester, New York)
W.P.T. James	(Aberdeen, Scotland)
Michael Lentze	(Bern, Switzerland)
John C. Waterlow	(London, England)
Elsie M. Widdowson	(Cambridge, England)
Vernon R. Young	(Cambridge, Massachusetts)

Three of us, Barness, Forbes, and Waterlow, have been members of the CSA since the Center was first set up 10 years ago. Another former member, Dr. Calvin Woodruff (Columbia, Missouri) died earlier this year, but not before he had made a valuable contribution to this report. A document on evaluation of research by the OECD[1] poses the question; "what is the point of carrying out an evaluation if at the end the impartiality of the evaluators is called into question?" In our experience it is unusual for a government-funded institution to have such a high proportion of foreign nationals among its advisers. We hope that this may help to promote impartiality. However, to the extent that our yearly reports have influenced the direction of the Center's work we are evidently not entirely impartial evaluators.

1.2. This report is in two parts. The first part was compiled in November 1988, and deals with the origins of the Center and its achievements in the 10 years up to that time, when the new building had just been brought into commission. No attempt has been made to bring this part up-to-date.The second part was initially drafted in February 1989, and is concerned particularly with future developments as we see them.

1.3. The Director proposed certain criteria for the objectives and scope of this assessment:

a) to evaluate the scientific performance and scientific standards;

b) to evaluate the relevance of the Center's achievements to its original mandate;

c) to comment on the organizational and administrative structure in so far as it affects the Center's performance.

Much of this report is descriptive because one cannot assess without a statement of what is being assessed. The descriptive part overlaps with numerous reports from the Director and the CSA and memoranda from the various parties concerned with the Center. Nevertheless, it may be useful to have this account from the perspective of outside scientists, particularly if the report has a wider circulation in the scientific community and is not confined to those already familiar with the CNRC.

The original mandate of the CNRC as laid down by the United States Department of Agriculture (USDA)/Agricultural Research Service (ARS) was to carry out research on the nutritional requirements of infants and children (to which mothers were added later), in order to promote the health and well being of this large and important section of the people of the United States. With this kind of mandate the "philosophy" of the Center has to lie midway between two extremes. At one extreme is the system, becoming less common in these days of public accountability, in which an outstanding individual is supported to develop his ideas as he thinks best. This is an extension of the traditional system of grants to outstanding workers in universities. At the other extreme is the kind of institution that is set up to provide answers to defined practical questions posed by sponsors in industry or government. In the intermediate situation the sponsors are able to put their questions only in general terms; it becomes the responsibility of the Director and the scientific staff to define the most relevant questions as well as to answer them. To achieve these aims, it is necessary to develop an appropriate balance between long-term and short-term research. These are heavy responsibilities and the task of the Director is more difficult than if, on one hand he were told, "We trust you. Get on with it," or if on the other, he were given a list of clear cut problems to be solved as soon as possible. We might call the three types of research philosophy: curiosity-oriented, mission-oriented, and problem-oriented. The CNRC is a mission-oriented institution. It is therefore perhaps the most important requirement of this report that we should try to assess the balance that has been achieved between long-term and short-term research aims.

It may be useful first to consider the organizational and administrative structures within which the research has to be done because they are bound to have an impact on this balance.

[1]Organisation for Economic Co-operation and Development. Evaluation of research: a selection of current practices. Paris: Organisation for Economic Co-operation and Development; 1987.

2. Organization and Administration

2.1. External Organization. The funds for the CNRC are provided by the USDA/ARS. In May 1985 the ARS signed a Cooperative Agreement with Baylor College of Medicine (BCM) setting out the responsibilities of each party. From the beginning Texas Children's Hospital (TCH) has worked hand in hand with BCM in the overall planning, in providing clinical facilities and in the leasing of the land for the new building. The initial planning group consisted of the President of BCM, the Director of TCH, and the Administrator of ARS. In March 1985, Dr. Kinney, Administrator of the ARS, wrote to Dr. Butler, President of BCM "I would like for you to know that the cooperation, trust, and support we have experienced in working with you and Dr. Nichols, Texas Children's Hospital, and Texas Medical Center Inc. has been outstanding and we want to continue to build upon that relationship." This is important testimony. The arrangement by which a government agency provides the funds for an institution of this size, but delegates the spending and administration of those funds to a nongovernmental body is unusual and perhaps unique. In 1985, Dr. Kinney stated, "We do not have a similar arrangement in effect anywhere in the country." Certainly in Europe large research institutes of this kind are generally funded and administered either directly by a government department or by a research council that is an organ of government. For example, in the UK the Medical Research Council and the Agricultural and Food Research Council; and in France INSERM. Since the CNRC arrangement has apparently operated well for ten years it can no longer be regarded as experimental and may well be a pattern to be followed elsewhere. We believe that all parties are to be congratulated on this outcome.

2.2. Responsibilities. The agreement of 1985 sets out the responsibilities of the two parties. BCM is responsible for administration and servicing of the Center. Up to now (November 1988), with one exception, BCM has been the employing authority for staff. This has enormous advantages: recruitment and employment by one of the leading medical schools in the country is a guarantee of quality and credibility. Moreover, since some of the programs involve work on sick children, medically qualified CNRC staff are able to use the clinical facilities of TCH. As regards the scientific work, BCM is responsible for maintaining high academic standards. However, the ARS maintains a close scrutiny, if not control, by the 5-yearly CRIS system, by which each individual project is defined and costed.

As of November 1988 there was one ARS staff member working in the General Services Unit of the CNRC. However, now that the new building is in operation, ARS is anxious to increase its own component in the Center. Over the next four years, there are plans to expand the ARS staff. These staff members will be recruited and appointed by ARS in consultation with BCM and the Director. ARS has the same aim in recruitment as BCM–to obtain original scientists who are capable of developing new ideas–and has a peer-review system to ensure this result. ARS recognizes that men or women of this caliber are unlikely to be recruited unless they see some opportunities for long-term strategic research.

The Director of the CNRC has the responsibility to ensure that an organization comprised of two groups of people with different employers and somewhat different terms of service, tenure, promotion, etc. does not lead to difficulties.

2.3. Internal Organization. In the early years, when the CNRC was lodged in the Medical Towers Building and the scientific staff was relatively small, there was little in the way of formal organization or structure. Under the overall authority of the Director three 'Laboratories' were established: Lactation under Dr. Garza; Weaning under Dr. Nichols; and Stable Isotope under Dr. Klein. Apart from these three senior people almost all the scientific staff were relatively junior and inexperienced in independent research. This initial structure was not particularly logical, because obviously there was overlap between the programs of the three laboratories. The work of the Stable Isotope Laboratory was clearly relevant to the other programs. There were some subjects which did not fit naturally into any of the three laboratories, such as body composition or gastrointestinal function.

Over the years the CSA consistently made two general recommendations: the need for closer collaboration and interaction between the scientists of the three laboratories, and the need to recruit more senior scientists. Two particular priorities were identified: a medically qualified senior staff member and a scientist experienced in metabolic and biochemical research. Progress has undoubtedly been made in implementing these recommendations. In 1985 the program and laboratory directors conducted a two-day retreat, in which focal areas of interlaboratory collaboration were identified. This appears to have produced a significant improvement in coordination. Now that the Center has moved into its new building, additional groups are being established and a major management review has taken place in 1989.

2.4. The Council of Scientific Advisors (CSA). The CSA established by BCM on the advice of the Director, first met in October 1979. At first it met twice a year, and since 1981, it has met annually. The CSA initially had four members, one of whom was from outside the USA. In subsequent years there has been some rotation and some enlargement of the Council and at recent meetings there have been guest advisors who are specialists in particular fields.

The main function of the CSA is to assess the research and to advise on future developments. However, its meetings have also been attended by senior staff of ARS and BCM. As a result the CSA has been kept fully aware of the administrative developments and has been encouraged to express views on organizational matters as well as on the scientific program. This free and open approach has been much appreciated.

The system of annual assessment as opposed to periodic site visits is perhaps somewhat unusual. It must impose a considerable strain on the Center staff, but it has the advantage that the members of the CSA get a good understanding not only of the research work and its progress, but also of the difficulties and problems. We hope that this has been useful, at least during the formative stages of the CNRC.

2.5. Buildings. The Center started as a small nucleus inside BCM and TCH. It then moved to temporary accommodation in the Medical Towers Building, and finally in its tenth year to the outstanding new building which embodies the tripartite collaboration described above. The following inscription appears at both building entrances:

CHILDREN'S NUTRITION RESEARCH CENTER
UNITED STATES DEPARTMENT OF AGRICULTURE
AGRICULTURAL RESEARCH SERVICE
in cooperation with
BAYLOR COLLEGE OF MEDICINE
and
TEXAS CHILDREN'S HOSPITAL

Several points about the building are important in relation to the scientific program. First, the Center as a building has developed in a natural way arising out of the science. There has been no question of putting up a building and then trying to fill it. Secondly, the physical proximity to BCM and TCH should improve collaboration at the scientific as well as at the administrative level. In this connection the Director of TCH has said, "We want to give not take." Thirdly, the planning of the building and the problems of moving and reinstalling delicate equipment have undoubtedly taken a great deal of time for the Director and staff and have inevitably produced some interruptions of scientific work.

3. The Overall Scientific Program of the Center

3.1. The mandate of the CNRC as laid down in the Cooperative Agreement is as follows:

That the mission of the CNRC is to conduct research that will lead to a definition of the nutritional requirements needed to ensure health in children from conception through adolescence, and in pregnant and lactating women. To accomplish this mission, the CNRC has the following objectives:

a) To determine how the diet of a pregnant woman affects her health and the health of the child she delivers;

b) To determine how nutrition of the mother affects lactation and the nutrient content of her milk;

c) To determine the relationship between nutrition and the physical and mental development and function of infants and children;

d) To define the nutritional needs for healthy growth through adolescence;

e) To develop noninvasive methods for investigation of the nutrient requirements of infants, children, adolescents, and pregnant and lactating women; and

f) To determine the biochemical, anthropometric and dietary standards for nutrition assessment of infants, children, adolescents and pregnant and lactating women.

At the outset as mentioned above, two main programs were initiated:

a) Pregnancy and Weaning Programs to determine nutrient needs from conception through the first year of life. Both mother and fetus/infant will be the focus of this effort.

b) A Lactation Program to establish the nutritional requirements for lactating women and for infants fed human milk.

It was envisaged that additional programs would be added later, specifically:

c) A Nutrition and Behavior Program to determine the consequences of early nutrition and later childhood dietary intakes on function and behavior.

d) Child and Adolescence Programs to determine the nutrient needs for normal growth and development through adolescence.

It is important to emphasize that this mandate does not include community surveys of nutritional status of dietary

intakes, etc., though exceptions may be necessary to provide a background for the scientific work.

3.2. The development of the Lactation Program has been relatively straightforward (see section 4). The Weaning Program, in contrast, has been somewhat heterogeneous, with three areas of primary focus: mucosal biology, hepatic biology, and protein metabolism. There has been a certain amount of overlap between the two programs, apart from the shared use of the facilities of the isotope and body composition laboratories. There are also a number of projects which do not fit well into either program except for administrative and technical convenience.

3.3. The basic scientific strategy has been to look at the problems set out in the mandate from the point of view of metabolism: that is, the interaction of food with physiological and in some cases pathological function. Metabolic research requires the use of tracers, which for studies on children and pregnant and lactating women must be stable isotopes. From the very beginning the development of a Stable Isotope Laboratory has been a priority and this laboratory is now recognized as one of the leading centers in the world for the application of stable isotopes to the study of human metabolism.

3.4. The composition of the body at any moment represents the end result of all the metabolic processes that have been going on. Therefore, much emphasis has rightly been placed on the development and use of methods for measuring body composition. The instrumentation for this work (e.g., ^{40}K counting, neutron activation analysis and total body electrical conductance (TOBEC)) is complex, bulky and expensive and it was not possible to take full advantage of modern technology until space became available in the new building. Of course, there are many parts of the research program that do not depend on these facilities. However, we mention them at an early stage in this assessment, because together they provide a unique opportunity for research on human subjects. There is, of course, always the danger that the tail will wag the dog and that projects will be designed not so much to answer questions as to make use of exciting new technology. This has indeed happened on occasion in earlier years, as pointed out in several of the CSA reports. However, such projects, even if they have little apparent relevance to the Center's mandate, may be justified if they are regarded as explorations of the capabilities of new technology and if they stimulate technical advances.

3.5. In the past the CSA has been concerned about excessive fragmentation of the work. Many projects were conducted which seemed to have little relation to the overall program or to each other and which have not led to the given goal. To a certain extent this sort of thing can be written off against experience and the need to allow younger workers to have their head in choosing and tackling a problem.

4. Survey of Research Achievements

4.1. It is not necessary for this ten-year review to duplicate the reports of the Director and the CSA, but some notes follow about areas in which we believe that significant progress is being made.

a) Energy Metabolism and Requirements of Infants. Measurements in both breast-fed and formula-fed infants of energy intake, resting metabolic rate, and total energy expenditure (by the doubly labeled water method) and storage (by acoustic plethysmography) suggest that energy requirements are substantially lower than current international estimates. This is clearly of great importance, particularly in relation to recommendations about the length of time for which infants could be exclusively breast-fed and the time at which supplementary foods should be introduced. The combination of these methods makes it possible to estimate the proportion of total energy expenditure that is used for physical activity by the infant, a subject on which, up to now, there has been virtually no information.

b) Functional Importance of Human Milk. It is generally accepted that "breast is best"; however, any differences between human milk and modern infant formulas reside not so much in the nutrient composition as in the presence of specific proteins and immune factors in human milk. The functions and metabolism of some of these proteins have been examined. Evidence has been produced that human milk stimulates the production of antibodies by the infant and that lactoferrin stimulates the maturation of the intestinal epithelium. Studies are in progress on the mechanism of this phenomenon and on the biochemistry and structure of lactoferrin. Comparisons are being made with lactoferrins from other species. This part of the program has developed very rapidly in the last three years and it is important to note that it relies heavily on animal models.

c) Utilization of Nutrients by the Infant. By feeding rice biologically enriched with ^{13}C it has been possible to obtain an extremely sensitive measure of the absorption and utilization of the rice starch. This kind of work will be extended when the new facilities come into operation for the biological labeling of natural foods. Research is also in progress on the extent to which the nature of the

cereals and of infant formulas may affect the absorption and utilization of dietary nitrogen, and perhaps of total energy.

d) Calcium and Phosphorus Requirements of Infants. It has long been a matter of concern how to provide adequate intakes of calcium and phosphorus for the low-birth-weight infant. Measurements of bone density have shown that with unfortified human milk calcium accretion is less than with fortified human milk or formula, although growth in weight and length were not affected. Even in normal infants increase in bone mass was less on human milk than on a commercial formula. These studies have been extended to miniature pigs and it has been shown that bone mineral content measured by single photon absorptiometry is a good marker for total body calcium. However, little attention has been paid to finding a good animal model for these studies (see section 5.4 below).

e) Factors Affecting Lactation. Thus far, attention has been concentrated primarily on the development and improvement of methods. The problem of accurately measuring human milk output is a perennial one. It was satisfactory to find that results by the labeled water method correspond well with those of careful test weighing in the metabolic ward. Studies have also been made on the effect of the fat content of the mothers' diet on the synthesis of milk fatty acids, using labeled water as the precursor. The results suggested an increased rate of milk fat synthesis in mothers on low fat diets. Further investigations with prelabeled fats have led to the important conclusion that when maternal fat intake is low, the total output of fat in milk is maintained by an increase in milk volume. Studies have been started on nitrogen balance and protein turnover in lactating women to characterize the adaptive responses of protein metabolism to the stress of lactation and their relation to maternal protein intake. Preliminary work has been done on the in vivo kinetics of milk protein synthesis.

f) Developments with Stable Isotopes. The use of stable isotopes has been an important component of most of the studies briefly reported in previous sections. It has to be recognized that these applications to biological problems represent the end result of long and painstaking work on methodology, on improving accuracy and sensitivity, while at the same time reducing the labor involved in the analyses. Perhaps the most impressive methodological advances have been in relation to protein turnover: the capacity to isolate and measure isotope abundance in extremely small amounts of free amino acids and proteins so that only microliter samples of blood are needed. These advances make it possible to study the kinetics of individual proteins as markers of nutritional state or stress. As may be suspected from earlier work on albumin, changes in turnover rate are likely to be far more sensitive than changes in concentration. A beginning has been made in this direction with studies on lipoprotein metabolism.

It should also be noted that the personnel of the Stable Isotope Laboratory provide a reservoir, not only of skill in instrumentation and analysis, but also of theoretical understanding of tracer kinetics. This understanding is essential for the proper application of tracers to biological problems.

g) Kinetic Studies of Amino Acid Metabolism. A major study has been conducted on lactating and postpartum women with the objective to estimate pool sizes and rates of exchange of amino acids between different body compartments. The protocol was extremely complex, involving a seven-pool model. Some differences, although not very large or clear cut, were observed between the two groups of women. This is probably the most sophisticated study in the field of amino acid kinetics that has ever been done anywhere. Perhaps its most important outcome has been to demonstrate the possibilities and the limitations of the approach. The results will help in the design of models that are simpler but still relevant. If this work is to continue, it might be more productive, as a next step, to use experimental animals for further exploration of these kinetic problems.

In another study on protein metabolism in lactating women, a much simpler protocol was used of the kind that has been developed and extensively used at MIT. The results showed some interesting differences between lactating and nonlactating women, but the numbers were too small to achieve statistical significance. Extension of this work must wait on the opening of the new metabolic unit.

h) Developments in the Measurement of Body Composition. This area of work started later than that on stable isotopes and is due for rapid expansion now that the new building provides facilities for ^{40}K counting and measurements by neutron activation. As can be seen from the summaries above, less complex instruments and methods are available and have been put to good use, such as acoustic plethysmography and the TOBEC method, as well as isotopic measurement of body water and analysis of bone density. It is recognized that one important component of the laboratory's work is and will continue

for some time to be the validation of these new instruments. This will be a major service, not only to the Center, but to the biomedical community at large, since it is well recognized that, particularly in pathological conditions, one approach on its own is not enough.

Whereas the phrase "body composition" usually implies the make-up of the body as a whole, it is also important, as the Center recognizes, to try to measure the amounts and growth of individual tissues, particularly bone and muscle. Because muscle forms a large proportion of body mass and particularly of body protein, it is appropriate that the work on body composition is being complemented by basic studies on the characteristics and determinants of muscle growth.

5. Future Developments

5.1. Staff. The space and facilities in the new building make it possible to fulfill the long expressed wish of the ARS to have more federal staff in the Center. This will also promote collaboration with other ARS Research Centers. Plans include the appointment of three ARS staff in the forthcoming year who will fit into the new programs described below, and it is forecast that the ARS staff will continue to grow. The departure of the Associate Director, Dr. Garza, will presumably lead to some reorganization of responsibilities and possibly the recruitment of new BCM staff. Since this report was drafted, Dr. Peter Reeds and Dr. William Heird have been recruited to the staff at a senior level.

5.2. Metabolic Ward. Since the CNRC was established, studies on infants and mothers under metabolic ward conditions have been an essential part of the CNRC's work. The twelve-bed unit in the new building provides the opportunity to expand this work and it is of concern that bringing it into operation is delayed by problems of funding and staffing.

5.3. Biological Labeling. The facility for growing plants on isotopically enriched media and so producing labeled foodstuffs has enormous potential for nutrition studies in man. It is expected that one of the new ARS staff members will be a plant physiologist who will direct this work. It is to be hoped that this will be much more than a service, and that basic contributions to plant physiology will emerge from this research. This aspect should be encouraged to make the post attractive to a first-class scientist.

5.4. Animal Facilities. It has always been the view of the CSA that the Center should make more use of experimental animals, particularly for the validation of kinetic models and of measurements of body composition. As one member of the staff has put it, "animal research in a human setting is best served by using it to examine general principles." One might turn this around and say that research on basic metabolic principles can only be prosecuted successfully when conducted on animals in parallel with the research on man. Until now, 85% of the Center's work has been on humans; the 15% on animals has been mainly in the areas of body composition and intestinal structure and function. The new animal facility is therefore a very important development. One can imagine, for example, that it would be much easier to study the metabolic adjustments determining the quantity and quality of milk during lactation by experiments on animals in the first place, and to derive from them markers for a way into the study of these processes in man.

It is essential, however, that the animal model chosen for any particular project should be appropriate. The pig, for example, is not an appropriate model for studies on the calcification of bone, and the rat may not be a good model, at least in some aspects, for research on the development of gut function.

5.5. Gastrointestinal Physiology. The profound influence of nutritional intake on gastrointestinal function in growing infants has clearly demonstrated the need for research on these two intimately related processes. For example, studies on intestinal mucosal repair, and of microvillus protein synthesis and turnover as a target of micronutrient action, will be fundamental to our knowledge of the development of metabolic processes within the gastrointestinal tract of a growing child.

5.6. Anemia and Trace Elements. Anemia is very common in infants and in pregnant and lactating women, but so far, the Center has not been able to do much work on it or on iron metabolism in general, except for the studies on lactoferrin already referred to. Investigations on trace element metabolism with stable isotopes are now a practical possibility and thought is being given to establishing a program in this area, particularly in relation to zinc and copper, perhaps in collaboration with the Grand Forks Center. This would certainly be a good development, provided that the human resources are available. Initial studies will focus on the metals as regulators of functional proteins.

5.7. Brain and Behavior. Work on this subject has long been on the agenda; it is included in the program specifically listed in the Cooperative Agreement of 1985. This is a particularly difficult subject because of the doubtful relevance of animal models to man, at least in regard to the psychological and behavioral aspects. This criticism does not apply if the point of attack is the study of the metabolism of substances that are important for the development and function of the brain,

using the approaches and methods that already exist in the Center. It appears that the time will soon be ripe for developing this program, because BCM in its future planning is giving a top priority to research in the neurosciences, including nutrition and the developing nervous system. There will thus be an opportunity for very fruitful collaboration.

5.8. Nutrition of Adolescents. This subject is the fourth program in the original mandate. Studies are now planned on changes in body composition during the adolescent growth spurt. It will be important also to give some attention to pregnancy in adolescent girls, and the effect on the newborn infant.

5.9. Community Studies. As mentioned earlier, it is not considered to be the function of the CNRC to conduct community surveys of food intake or of nutritional status. These are matters for other agencies, such as the USDA, FDA, Public Health Service, and CDC. However, when a problem has been identified by epidemiological means, then it becomes appropriate for the Center to initiate research on its causes and characteristics. A good example of the identification of a target group with a specific problem is that discussed by the Director at the 1987 session of the CSA: "What are the causes of low birth weight and high infant mortality in the black population in Houston?" Even if the causes are socioeconomic, the end results–low-birth-weight and death–must be produced by metabolic mechanisms.

6. Conclusions

6.1. Scientific Merit. Ten years may seem a long time, and some 400 a large number of publications to have been produced during that time; nevertheless, it would be premature at this time to attempt a conclusive assessment of the scientific quality of the work. It is not an easy task to achieve a program that is integrated towards the fulfillment of a mission, but that also allows the intellectual freedom necessary for productive research. Such a task takes time. The Center is young; of 26 scientists now in posts (as of November 1988), only eight hold senior appointments (Associate Professor and Professor). Six of these have been in the Center for five years or more; that is not very many. These factors must be borne in mind in our assessment.

a) The work on energy metabolism and the requirements of infants has achieved wide international recognition. This work is timely, because there is much concern about the subject, but little in the way of hard information. An infant's energy requirements have to cover his needs for maintenance, thermogenesis, balanced growth, and physical activity. This research provides the soundest basis that has been achieved so far for dissecting out these components of the requirement. In studies of this kind it is invariably found that infants do not always behave in the same way. They have different intakes, grow at different rates, and put on different proportions of fat and lean tissue. These relationships have never been properly explored and detailed studies over a fairly long period in a metabolic ward should throw much light on them.

It should be noted also that the physical activity of infants is probably of great importance for their mental and behavioral development; and the ability to measure accurately this component of energy expenditure, if it is exploited, will be a significant step forward.

This is a growth area from the scientific point of view, and from what has already been accomplished, it can be foreseen that the CNRC will occupy a leading place in this field.

This work has been meticulously done with the back-up of advanced methods. It would be too much to claim that such a line of research represents an intellectual breakthrough, because the underlying questions are straightforward and clear, but it is of great practical use. The work has benefited greatly from having been pursued consistently and steadily over several years.

b) The second area in which the CNRC may rightly be said to be famous is that of stable isotopes. Here the position is different. As is evident from Section 4 of this report, many useful pieces of work have been done, but there does not seem to be any unifying concept. It might be said that stable isotopes are a tool which can be applied to many different kinds of problems, so that no general concept is necessary. This would be a mistake; the importance of tracers is that they make it possible to measure rates of exchange of materials in the body. This can be done in no other way except at the most elementary level, as by balances. The challenge therefore is to develop metabolic models and hypotheses that can be tested and quantitated by tracer methodology. The importance of the methodology is that unless it is available, models cannot be explored and hypotheses tested, and it is a waste of time devising hypotheses if they are not testable. One example of a response to what we have called the challenge of stable isotopes, is the study summarized in Section 4.1 Paragraph (g). The main reason that there has not been a greater and more continuous effort in this area has been the difficulty of recruiting a staff member capable of making the necessary input from the metabolic side. Such people are not

common, but we hope that this deficiency has now been overcome with the appointment of Dr. Reeds.

It would be wrong not to give credit to the other contributions, actual and potential, of the Stable Isotope Laboratory. Of particular importance is the measurement of total energy expenditure with doubly labeled water, which represents a breakthrough in nutritional science. The concept was developed some 40 years ago, but it is only in recent years that it has been possible to apply it to man. A number of laboratories in Europe, as well as in the USA, are working on this subject, but several theoretical problems remain. The Stable Isotope Laboratory is making a significant contribution to the validation of the method and we presume that they will be using it more widely in the future.

Lastly, the biological labeling of plant materials which has just begun has an important future. Some studies of this kind have been done in man in the UK and in East Germany with biologically labeled eggs, wheat, and yeast, the first of them more than 30 years ago, but in neither country has this approach been developed in a systematic and comprehensive way. Apart from the practical problems of getting the isotope into the desired plant components, there are some theoretical difficulties to be overcome, in that the amino acid composition of these materials differs from that of human body proteins. However, it may be confidently expected that in a few years the CNRC will be a world leader in this field.

c) A third area in which notable scientific advances are being made is in the immunological components of human milk and their effects on tissue function. The studies on lactoferrin, although in a fairly preliminary stage, are innovative and interesting. This approach is capable of being extended to the effects of infection on tissue metabolism and how the infant copes with them.

The fact that three areas of the CNRC research have been picked out for special comment does not mean that other components of the program are not successful and useful, but most of them have not yet been developed on a broad enough front to achieve the scientific recognition that we are trying to assess.

Practical Implications. It is appropriate at this stage to use the word "implications" rather than "applications." The latter suggests that there is a precise practical question to which new knowledge can give a precise answer. In fact, however, the ARS mandate, as set out in Section 3 Paragraph 1, is couched in very general terms. If there are to be practical applications, it is necessary as the work goes forward to isolate questions from each section of the mandate that are defined and answerable. What we are concerned with at this stage is the background knowledge that will make it possible to answer such questions when they are formulated.

The subjects on which new knowledge is being gained which have practical implications may be listed very briefly:

- Infants' energy requirements in relation to health and growth.
- The partition of energy expenditure in infants.
- Comparison of the effects on growth and energy expenditure of human milk and commercial formula.
- The practicability of fractionating human milk proteins and the effect of enriched human milk on growth in low-birth-weight infants.
- The significance of the immunological components of human milk.
- The effect of different feeding regimens on bone mineralization in infants.
- The capacity of the infant to digest starches.
- The influence of maternal diet on the composition and quantity of her milk.

7. SUMMARY OF CONCLUSIONS

7.1. There has been extraordinarily good cooperation over ten years between the three main parties concerned with the operation of the CNRC: ARS, BCM and TCH.

7.2. As a consequence the unusual and innovative arrangement under which the Center operates may be regarded as highly successful and hopefully as a pattern for other initiatives.

7.3. Very great credit is due to the Director for what he has accomplished in the setting up, organization, and scientific direction of the Center.

7.4. We strongly support the emphasis placed by both BCM and ARS on the importance of basic science in the Center.

7.5. It has not been easy to recruit senior staff of adequate caliber to fulfill the very wide mandate of the ARS.

7.6. There have been difficulties and weaknesses in scientific management and coordination, but these are being overcome.

7.7. The general atmosphere in the Center appears to be one of enthusiasm and job satisfaction.

7.8. The emphasis on advanced technology is justified, but full use has yet to be made of it.

7.9. Overall, the productivity of the Center has been substantial. A satisfactory proportion of the work can be rated as of high scientific caliber by international standards.

7.10. Many significant contributions have been made to the solution of practical problems in the field of infant nutrition.

7.11. There is a better awareness of the need for supporting research on human beings with studies on experimental animals.

7.12. Now that the teething troubles of the Center have been largely overcome, increasing efforts should be made to develop collaboration and cross fertilization with BCM at the scientific level.

7.13. To the extent that the ARS mandate allows, thought should be given to a greater involvement with training, particularly at the postgraduate level. An appendix on this subject is attached (Appendix I).

7.14. A second appendix is attached on international activities (Appendix II).

7.15. Exciting new developments can be foreseen over the next few years.

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PART II. Future Developments

Part I is a factual account of what has been achieved, with some expression of our opinions. In Part II we are more concerned with strategic issues for the future.

1. Research Strategy

1.1. The CNRC's mandate sets two boundaries to its program. The first is to work on nutritional questions of public importance. The second is that, as must other USDA Centers, the CNRC is mandated to carry out research on the nutritional problems and needs of supposedly healthy people. Research on the sick is the responsibility of the NIH. This division makes sense administratively, but in practice it has to be interpreted with some flexibility. Processes in normal people are in almost all cases the result of an equilibrium. It has been said that in order to understand an equilibrium you have to disturb it. For example, our understanding of normal cholesterol metabolism and its control can gain immensely from studies of familial hypercholesterolemia, and understanding of normal gut function is illuminated by work on intestinal disease. We have the impression that the ARS is sympathetic to the concept that in research on man it is not possible to make a hard and fast division between normal and abnormal.

1.2. In Part I we referred to the classification of research as problem-oriented, mission-oriented, and curiosity-oriented. By its mandate, the CNRC program falls in the first two categories. It is possible that the interests of the two sponsoring organizations could pull in opposite directions. The ARS wants answers to questions that affect the health of the nation's children. BCM wants to see the Center internationally recognized as the leading institution in its field, and this is difficult to achieve without a measure of curiosity-oriented research. However, the ARS, greatly to its credit, has made it clear that it is interested in good science and that it will never seek to limit the activities of a scientist who wishes to pursue a problem to the end.

The question of freedom of choice within the mandate is also important from the point of view of recruitment of staff and their scientific development. Some people find their satisfaction in tackling clear-cut practical questions, others in delving deeper into a theoretical question, regardless of where it may lead them; some flourish best when they are able to pursue both kinds of activity at the same time.

It is the Director's responsibility to achieve a balance both of programs and of staff. This is a difficult task. In our view the Director's personal qualities and experience have enabled

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him to make good progress in this. He has a commitment to the well-being of children and also to the encouragement of basic research. However, there is still some way to go.

1.3. Another way of classifying research that may be helpful relates to the biological level at which it is done. The first level is observational and much of the Center's work falls into this category.

Examples would be the research over many years on intake, growth and energy expenditure of infants, with special attention being given to better methods of measurement. To call such studies observational is not in any way to decry their scientific value. Eight years after the last UN committee on energy and protein requirements, we realize very clearly how inadequate our knowledge was at that time in relation to infants and young children. Work that will help to fill those gaps is extremely important, and the CNRC is in a unique position to support it with the most up-to-date and accurate methods of measurement. All these functions have a wide range of variation. An important direction of work for the future is to increase our understanding of the outliers, which may be identifiers of genetic variations.

The second level is that of processes, which in this context means metabolic processes. Here research is aimed at understanding not only what happens, but how it happens. As mentioned in Part I, from the very beginning a large part of the Center's research has been of this kind, and it is here that the use of stable isotopes comes into its own. We have already mentioned our very strong support for a major emphasis on metabolic research and we believe that both ARS and BCM agree with this view.

The third level is that of cell biology. A certain amount of the Center's work comes into this category, e.g., that on lactoferrin and on the intestinal epithelium. The work on the development of muscle fiber types during development is moving in that direction.

1.4. The question has been raised by several people: should not the CNRC be doing more research at the molecular level? If it does not do so, can it ever achieve a position of world leadership? Is it not missing an opportunity both for developing its own initiative in this area and for collaborating with other groups in the Houston area? These are valid questions.

It is not realistic for a Center such as the CNRC to consider molecular biology in vacuo. Its methods have to be applied to biological problems relevant to nutrition. It is likely that the differences between individuals referred to above have a genetic basis. Only in a few cases, such as hypercholesterolemia, do we know anything about the genetic control of metabolic and nutritional characteristics. Even less is known about how nutritional factors influence gene expression. Looking to the future, it might be appropriate for the scientists in each program to examine with molecular biologists at BCM and elsewhere how their approaches and techniques could be applied fruitfully to problems within the Center's mandate.

The subject of molecular biology, to be prosecuted successfully, requires a certain critical mass. In determining priorities for the future, account obviously has to be taken of the resources and staff posts available. The scope of the CNRC's work is already quite wide (see Part I), and it might be a mistake at this stage to enlarge it even further. The way ahead for the time being probably lies in closer collaboration with molecular biologists at BCM.

It must also be emphasized that a main concern of nutrition as a science is with the integrated function of the whole organism. This is an area as challenging and difficult as any in biology, but at present, it is a relatively neglected branch of the biomedical sciences. The CNRC is in good standing in this field, and this should not be jeopardized.

2. Research Management

2.1. The Director. All directors of sizable organizations have a style of their own and a vision of their own. It is no good expecting a director to be all things to all men. Someone who has the drive to build up something new does not necessarily have all the different talents needed for day-to-day administration.

The functions of the Director of the CNRC, as we see them, are:

a) To maintain the right balance between the expectations of the ARS and BCM, and correspondingly between problem-oriented and curiosity-oriented research. This is a very difficult task. We have heard it said that Dr. Nichols inclines too much towards the ARS, but after all, this is the source of his funds.

b) To recruit senior staff of high caliber. The CSA has followed his attempts to do this over the years and recognizes the difficulties.

c) To develop collaboration with other institutions in the region.

d) To maintain an internal management structure that promotes the most effective use of the scientific manpower and physical resources of the Center.

2.2. Management Structure. Up to the time of the last CSA visit there had been little, if anything, in the way of a formal management structure. In the early days, as said in Part I, the Center's research was divided into three programs: Lactation under Garza, Weaning under Nichols; and Stable Isotopes under Klein. Each head of program apparently had a good deal of autonomy. The division was a somewhat artificial one, and with the widening scope of the work, such a simple structure is clearly no longer adequate. It is impossible for the Director himself to be fully acquainted with the technical details in every area. It is also unlikely to be satisfactory to have a structure that consists simply of a number of senior scientists who are severally and separately responsible to the Director. Although the CNRC is a mission-oriented institute and its staff are working to a common end, they can have considerable academic freedom. Good scientists, if they have the opportunity to be creative, will tackle the big issues of concern to the ARS, while at the same time fulfilling their urge for deeper enquiry. However, a mission-oriented group has to be cohesive. There needs to be some system or structure for integration of research programs.

We perceive the following functions for a research management system:

a) To promote collaboration and cooperation between individuals and groups in the CNRC.

b) To examine research programs and protocols from the point of view both of the science and the resources needed, and to advise the Director accordingly.

c) To advise the Director on the career development of staff.

d) To organize seminars, workshops, and information services and contributions to teaching.

e) To ensure that higher degree students are being properly trained.

It is unlikely that all these functions can be exercised by a single group or committee. The important point is that the functions should be identified. It is not for us to suggest exactly how they should be implemented.

2.3. Development of Protocols. (Function 2 above). This process represents the tactical implementation of an agreed strategy. The CRIS system is a management tool of the ARS and the CNRC has to fit in with it. Each program or project has to have its CRIS, which operates for three years with a possible extension to five years. The ARS arranges for peer-review of the CRIS proposals before they are approved. About 12 CRIS proposals cover the whole work of the Center. It is important that they should be flexible, so that they can accommodate new ideas which come up within the period. We understand that Drs. Klein and Reeds have formed an ad hoc group responsible for organizing the new proposals that have to be presented this year. We have been told that this arrangement is working well, from the point of view of both the Director and the research staff. This 2-man group appears to be forming the embryo of a management system.

2.4. In any organization there are almost always problems in the relationships between people, and the CNRC has had its share. A number of people have expressed the view that Dr. Nichols is a difficult man to work with. This is often the case with anyone who has a capacity for leadership, is single-minded in achieving an objective, and therefore is liable to have blind spots in other directions. As we have said above, every director has his style. Some colleagues will be stimulated by it, others may find it difficult to work with. Perhaps the most important function of a management system is that it provides a framework, if not for solving, at least for limiting the damage caused by interpersonal difficulties.

3. The Role of the Clinicians at the CNRC

3.1. For many years the CSA has been saying that the CNRC should recruit a senior clinician who also has an established reputation in research. The appointment of Dr. William Heird, a distinguished neonatologist, is therefore most welcome. Nevertheless, because of the somewhat unusual relationship between the CNRC and BCM (see Part I of this report) some further examination is needed of the role of medically qualified staff in the CNRC.

3.2. A metabolic unit for the study of normal people must be, and must be seen to be under medical supervision. This is particularly important when the subjects are infants or pregnant and lactating women. Metabolic units operating outside the physical confines of a hospital are few and far between, both in the USA and the UK. As far as we know such a unit specifically for children is unique. It is necessary notwithstanding that TCH has a metabolic unit of five beds. That unit has to fulfill the needs of all TCH staff and could not accommodate the flow of subjects required for longer term studies on healthy children.

Granted the need for a separate unit at the CNRC, the medical cover is already most competently provided by Dr. Motil, who is well accepted as a clinician by TCH and who has a good deal of relevant research experience. This, therefore, is not the rationale for the need expressed for another senior clinician.

3.3. Apart from Dr. Heird, who has not yet started here, the four medically qualified members of the CNRC staff spend a designated part of their time in service work at TCH. They take care of patients referred to them by colleagues or general practitioners and part of their salary is covered by these patients' fees.

There seems to be a curious lack of relation between their service work at TCH and their research work at the CNRC. Unlike the usual clinical research workers, whose beds and whose laboratories form a continuum, they are in effect doing two different jobs in two different places.

As far as we know, problems of individual sick patients, e.g., gastrointestinal function, are not studied within the confines of the CNRC nor are the methods of investigation developed at the CNRC applied to patients in the hospital (with the exception of Dr. Klish's measurements of body composition, but this work does not represent a real interinstitutional research project).

One reason for this somewhat anomalous state of affairs is that the ARS mandate does not often encourage research on sick children.[2] However flexibly this mandate is interpreted, it would not be medically possible to admit children to the CNRC metabolic unit at a time when they were actually ill. Even premature babies cannot be studied there. However, we do not believe that this is the only reason. Clinical research workers have various motivations. Some are primarily interested in patient care, but also have the curiosity to follow up problems presented by their patients. For these, a post in a medical school is probably the most appropriate. Others see themselves mainly as biomedical scientists who continue to do some clinical work, either as a source of research opportunities or out of a sense of practical service and a source of job satisfaction. It is people of this kind whom the CNRC should try to recruit. Unfortunately, from what we have been told, at the present time individuals with this kind of motivation are hard to find.

Nevertheless, if the resources of the CNRC are to be fully used, it is essential to maintain the search for younger clinical investigators. Even if there are no posts, it is to be hoped that grants from the NIH or other agencies would be available. This is a long-term policy, which should be prosecuted in close collaboration with BCM. Without that, it is doubtful whether the policy can succeed. To the extent that it does succeed, it will strengthen the ties between the two institutions. We consider it very important to add scientific substance to the formal relationship described in Part I of this report.

4. Function of the CSA

4.1. Originally, it was not clear whom the CSA (then called the Board of Scientific Counselors) was meant to counsel or advise–whether the Director, the ARS, BCM, or all of them. In recent years, the situation has been clarified. The ARS has its own system for monitoring the progress of the USDA research centers. The CSA is now advisory to the Director, who, as far as we know, is solely responsible for appointing its members. There is no fixed term of membership. Three of the current members (Barness, Forbes, and Waterlow) have served for the past 10 years. Some of the initial members have dropped out and been replaced by new ones (James, Lentze, Widdowson, and Young). Guest advisers may be invited to attend a particular meeting in order to enlarge the scope of the advice.

All the members of the CSA have now offered their resignation, in order to allow the Director to make a clean sweep and build up a new system if he so wishes.

4.2. The annual meetings of the CSA have in general fallen into three parts:

a) Presentation of numerous short reports by the CNRC staff.

b) Informal discussions between the CSA and the ARS staff.

c) Private meeting of the CSA at which the main lines of their report are discussed.

There have been a number of criticisms of the detailed format of the meetings, but it is not necessary to go into them here.

4.3. For the future it is up to the Director to decide whether or not he continues to want an external advisory body. If he does, we make the following suggestions on the basis of our own experience:

a) The Council should be set up and operate in such a way that it is recognized as independent and regarded as useful by the ARS and BCM. It would be highly

[2] The Food Security Act of 1985 reiterates the policy that "designates the Department of Agriculture as the lead agency of the Federal Government for human nutrition research (except with respect to the biomedical aspects of human nutrition concerned with diagnosis or treatment of disease)..."

desirable for the Council to include one member of the BCM staff appointed not as a representative of Baylor, but because of an interest in nutrition.

b) There should be a clear distinction between long-term advice on strategy and advice on the usefulness and scientific merits of particular projects, although, of course, there is an overlap. These two kinds of advice require rather different kinds of people: in the first case, general experience in the field of nutrition research, combined with experience or responsibility for an institute or department; in the second case, up-to-date knowledge of relevant scientific fields.

c) We are not certain whether the CSA has, in fact, been useful over the last 10 years. However, it seems reasonable that a young institution, with an unusual administrative structure, which has grown very fast, could get some benefit from the views on strategy from an independent group. The majority of the present CSA members consider that annual meetings are valuable, provided that there is reasonable continuity of membership.

d) Technical meetings to review one or more programs should be organized separately, but it would be useful if one member of the Council who has experience of the subject could attend each meeting and report on it at the meeting of the Council.

5. Conclusions and Recommendations

5.1. The CNRC appears to be achieving its mission through an appropriate mix of strategic and applied research.

5.2. It is essential that the Center develop a clearly defined system for research management. We are not here concerned with administrative and financial management.

5.3. Every effort should be made to develop closer scientific links with BCM. If they led to work that was outside the mandate or mission, presumably they would be separately funded.

5.4. Efforts should continue to build up and train a cadre of young clinically qualified research workers.

5.5. If a Council of Advisors continues to exist, a clear distinction should be made between strategic advice based on experience, and scientific advice on particular programs.

5.6. We put on record that it has been a privilege for us members of the CSA to have played a part, however small, in the development of this important Center. We thank the Director and his staff for the time they have given us in the preparation of this report, and Norma Hayley, who translated it into the present final form.

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Appendix I Education and Training

Graduate Education

The cooperative agreement under which BCM operates the CNRC for the USDA states that "outside parties such as visiting professors, predoctoral, or postdoctoral trainees, may apply to conduct research with a nutrition variable at the Center. Such outside parties must be approved by BCM in accordance with its policies and procedures. Applications will be held in confidence and be subjected to an equitable peer review by BCM and CNRC. Authority to accept an application resides in BCM after discussion with ARS."

Education is a major component of BCM's responsibilities. As of 1987, BCM had awarded 342 Ph.D. degrees and 176 M.S. degrees through its graduate school. There are 11 Departments, Divisions, and Programs of the College which offer approved Graduate programs leading to the Ph.D. degree.

A program leading to a Graduate Degree in human nutrition was proposed in 1987. This proposal received a careful review from the ARS National Program Staff, Dr. Gerald F. Combs. Dr. Combs believed that a Graduate Program in human nutrition at BCM was appropriate for the Graduate School and could be offered through its Department of Pediatrics, but that it should not be considered to be a program of the USDA Children's Nutrition Research Center. The ARS is a Research Agency and not authorized to support education and training activities per se. Graduate students can be employed to help conduct research under the direction of qualified scientists, and by so doing, gain most valuable research training. This is appropriate and is done at most ARS laboratory locations. The ARS is keenly aware of the need for research training programs, but the ARS role in the Baylor Graduate School program in human nutrition must be limited to the research opportunities for students employed by the CNRC on appropriately approved research projects.

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Care should be taken not to refer to the program in Human Nutrition Graduate Education as a CNRC Graduate Training program, since it indeed must be kept separate as a Baylor College of Medicine program. The Center should be thought of as a place where students may receive research experience while enrolled in the Baylor program. Dr. Combs could see no reason why the critically important facilities and research opportunities should not be described as part of a Baylor College of Medicine graduate program. This applies to dissertation research which could be carried out under the direction of graduate research staff of the Department of Pediatrics. All graduate faculty at the CNRC have appointments in the staff of the Department of Pediatrics.

Additional reasons that the USDA Children's Nutrition Research Center should be kept separated from the formal graduate training programs were listed as follows:

(1) Research scientists employed by the Center and teaching graduate courses should either a) show that they are engaged in USDA supported activities for at least 40 hours per week with teaching time in addition to that, or b) receive a portion of their salary from another source (training grant BCM).

(2) No USDA funds can be used for graduate student tuition.

(3) Since the Center is housed in a USDA building, use of rooms for academic teaching purposes may not be necessarily allowed and if so, overhead charges might need to be considered.

(4) The House appropriations language in 1986 on page 32 states, "the committee recognizes that the Human Nutrition Research Centers can play a major role in the training of students in the field of nutrition research. To the extent practicable, the Centers should support nutrition and health sciences graduate student research and education programs with their resources and facilities."

With this background, scientists in the CNRC prepared a proposal for a graduate program in human nutrition and submitted it to the Dean of the Graduate School in 1987. The proposal received a critical review and two valid issues were raised.

The first was that there were no CNRC scientists with extensive experience with Graduate Education or in the management of Graduate Education. The second issue was that the CNRC is a component of a clinical department. There has not been a tradition of graduate degrees offered in clinical departments at Baylor College of Medicine. This report was received at the time of the move into the new CNRC facility. For this reason, further activity concerning the establishment of a Baylor College of Medicine program in human nutrition graduate education was postponed until a satisfactory completion of the move.

At the present time, a CNRC Committee of Graduate Education has been appointed and it is anticipated that the development of a graduate program will be critically important in the future recruiting of Senior CNRC investigators. Most candidates for appointment to the CNRC are participating in graduate education in their present academic positions and the presence of a strong graduate program in human nutrition would be an important factor in their consideration of a move to the CNRC.

Medical Student Education

Since 1971, the CNRC staff has provided an overview elective course, Basic Principles of Nutrition, for medical students. Participation in these courses has varied and in some years the course has been presented twice. It is an eight-week course; two hours of lecture and two hours of rounds/practicum are presented weekly. Unofficially, the count of students having enrolled in the course is 360. In 1986, as a result of this course, students "surveyed" their peers and unanimously requested that the study of nutrition be included in the core curriculum. No such core nutrition curriculum exists at BCM at present.

The clinical elective in Pediatric Gastroenterology and Clinical Nutrition is available to students who have completed their pediatric core rotation; usually 4th-year students elect this course. This elective is coordinated with Dr. Klish at TCH. An unofficial count of students who have elected this course is thirty-five, which includes students from other medical schools. The course is available to those students from other medical schools who have been awarded the American Medical Association Education and Research Foundation Scholarship in Clinical Nutrition.

Postdoctoral Program

In keeping with the cooperative agreement, referred to above, and with the understanding that the Center is authorized to carry out research training (this word appears in the title of the Cooperative Agreement), the program in postgraduate nutrition education of pediatricians has continued with the development of the CNRC. Initially, the program consisted of one or two years of research training following a clinical year for pediatricians who wished to specialize in gastroenterology and nutrition. The program was opened up to neonatologists coming from the same environment. The

program now consists of two years of laboratory or metabolic unit research, after one year of specialized clinical experience in nutrition and gastroenterology or neonatology. The agreement provides that these individuals work within approved CNRC projects and under the supervision of a CNRC scientist. In this regard, it is useful to note that the American Board of Pediatrics is now standardizing all pediatric fellowship training to include 2 years of laboratory or metabolic ward research experience. A similar requirement is stated by the American Board of Nutrition.

In addition to M.D. postdoctoral trainees, a number of Ph.D.s have undertaken postdoctoral training in the Center. This has proven to be an important tool for the recruiting of young scientists into the CNRC staff. Drs. Nancy Butte, Marta Fiorotto, and Douglas Burrin are examples of this mechanism of postdoctoral training and recruitment.

There have been problems concerning the quality of research carried out by some postdoctoral trainees. These people continue to have clinical obligations, such as clinics twice a weeks and night calls and weekend coverage, which disrupt the intensity of laboratory investigations. Efforts have been made to resolve this issue by simplifying clinical obligations when these postdoctoral fellows are assigned to work under CNRC scientists. The problem, while improved, still exists. On the other hand, neonatology fellows, when assigned to work in the CNRC, are almost completely free of outside obligations. While not all fellows have succeeded in developing a line of research within an existing project statement, those who have been successful have done very well.

In looking to the future, it would be helpful if postgraduate trainees in Obstetrics and Gynecology, Adolescent Medicine, and Internal Medicine could be recruited. The postdoctoral program is now organized under a CNRC committee.

The quality of applicants has improved remarkably in the last three years. It may be that a more aggressive recruitment strategy for quality applications would result in a better selection of clinical and nonclinical postdoctoral students with a long-term commitment to nutrition careers as an important contribution to improving the number of clinical faculty with background and experience in human nutrition research.

Comment

This Appendix is a slightly abbreviated version of a statement provided by the Director.

The CSA strongly supports these activities in education and training and appreciates the efforts that have been made by the ARS and BCM to define their respective responsibilities.

It is never satisfactory for research to be entirely divorced from training. For the research worker, training provides a rewarding and stimulating experience, provided the load is not too great. For the trainee, the arrangements described here provide a unique opportunity.

We have already mentioned the difficulties of recruitment, particularly of clinical staff. The activities described in this Appendix are the best long-term solution to this problem.

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Appendix II
International Activities of the Children's Nutrition Research Center

Statement by the Director

The CNRC was established in the section of Nutrition and Gastroenterology of the Department of Pediatrics in 1978. This group had established a precedent of international research collaboration which included work in Jamaica, Mexico, and Guatemala.

This was one of the issues discussed at the site visit to the CNRC in 1977, when Congress was reviewing the feasibility of establishing the CNRC. During the period of CNRC development, there have been several experiences in international collaborative research. One such study was an investigation of body composition in potassium-depleted infants in Brazil. Another was an investigation of body water spaces in growth-stunted children in Peru.

Ongoing studies include an investigation in human milk-fed infants with failure to thrive, which is taking place in Capulhuac, Mexico. A study in Brazil of mucosal atrophy in malnourished children is funded by a grant from Bristol-Myers. The disorders of colonic fermentation are being investigated

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in these same children under support from the ARS. There has been specific collaboration with INCAP in Guatemala concerning the digestibility of rice cereal in infants recovering from diarrhea. This important investigation addresses the appropriate method for refeeding children in the developing world who are recovering from diarrhea.

All of these investigations have addressed a specific line of inquiry within the context of an approved CNRC/ARS project statement. Of the many CNRC collaborations that exist, both inside and outside the United States, all are of this nature.

The CNRC and the ARS are not granting agencies. Collaborative research is specifically focused on the accomplishment of the research mission of the Center and the Agency. Consequently, there is no opportunity to provide long-term sustaining support for international research centers. The CNRC has cooperated in a short-term collaboration by providing specific equipment to the investigation of vitamin D metabolism in infants in China. It is possible that this precedent could be expanded in the future to address issues of low birthweight and specific micronutrient deficiencies in selected populations of the developing world.

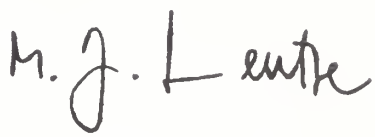
Within the context of international research, Dr. Floyd Horn (ARS), has stated that scientific objectives would determine which populations, either inside or outside the United States, would be studied. There may be times when a population outside the United States, one with unique nutritional characteristics, can serve as an appropriate reference population. This does not require a highly visible "international initiative." These reference populations will enable objective comparisons with the Benchmark population currently under investigation at the CNRC.

Comment

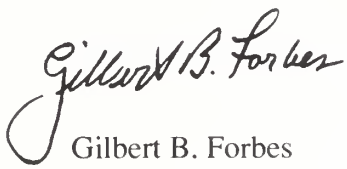
We regard these activities and the philosophy and administrative arrangements under which they are carried out, as appropriate and useful. They represent an extension of the principle that, in order to understand the "normal" (in this case the healthy child population of the United States), it may sometimes be necessary to study the abnormal (sick children) or children and their mothers living in an entirely different environment.

After our review of the first ten years of research and administration of the Children's Nutrition Research Center, we respectfully submit this report.

Lewis A. Barness

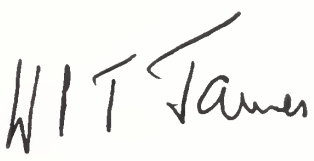


Michael J. Lentze



Gilbert B. Forbes

Elsie M. Widdowson



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November 5, 1989